

Exhibit A in support of the declaration of Dr. Freeman

CURRICULUM VITAE
University of Pittsburgh
School of Medicine

BIOGRAPHICAL

Name:	Bruce A. Freeman, PhD	Birth Date:	5 April 1952
Home Address:	5801 Wilkins Avenue Pittsburgh, PA 15217	Birth Place:	Akron, Ohio
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EDUCATION AND TRAINING

UNDERGRADUATE:

Dates Attended	Name and Location of Institute	Degree Received/Year	Major Subject
1970-1974	University of California	Bachelor of Science, 1974	Biochemistry

GRADUATE:

Dates Attended	Name and Location of Institute	Degree Received/Year	Major Subject
1978	University of California, Riverside Dissertation Title: The Reaction of Ozone with Human Erythrocytes and Model Membranes	Ph.D., 1978	Biochemistry

POST GRADUATE:

Dates Attended	Name and Location of Institute	Name of Program Director and Discipline
1978-1982	Departments of Biochemistry and Medicine Duke University Medical Center, Durham, North Carolina	Irwin Fridovich, PhD James Crapo, MD Redox Biochemistry

APPOINTMENTS AND POSITIONS

ACADEMIC:

Years Inclusive	Name and Location of Institution/Organization	Rank/Title
1978-1982	Duke University Medical Center, Durham, NC Departments of Biochemistry and Medicine	Postdoctoral Fellow
1982-1985	Duke University Medical Center, Durham, NC Department of Medicine	Research Assistant Professor

1985-1990	The University of Alabama at Birmingham Birmingham, AL. Departments of Anesthesiology, Biochemistry and Molecular Genetics	Associate Professor/Tenure
1990-2005	The University of Alabama at Birmingham Birmingham, AL. Departments of Anesthesiology, Biochemistry and Molecular Genetics and Pediatrics	Professor
1996-2005	The University of Alabama at Birmingham Birmingham, AL. UAB Center for Free Radical Biology	Director
1999-2005	Department of Environmental Health Sciences The University of Alabama at Birmingham	Professor
2006-	Department of Pharmacology University of Pittsburgh	Professor and Chair

MEMBERSHIPS IN PROFESSIONAL AND SCIENTIFIC SOCIETIES

Organization:

American Association for the Advancement of Science
 American Chemical Society
 American Heart Association
 American Physiological Society
 American Society for Cell and Molecular Biology
 American Thoracic Society
 Biochemical Society
 Co-Founder-Oxis, Inc., Portland, OR
 Founder-Nitrolipids, Inc. Birmingham, AL
 Society for Free Radical Biology and Medicine

HONORS

Year	
1993-present	Professor Ad Honorem, Facultad de Medicina, Universidad de la Republica, Montevideo, Uruguay
1995-1996	President - The Oxygen Society/Society for Free Radical Research
2003	Designated ISI Highly Cited Author – Biology and Biochemistry
2006	Designated Irwin Fridovich Professor of Pharmacology

FELLOWSHIPS AWARDED

Year	
1981	Queen's Quest Visiting Scholar, Department of Pediatrics Queen's University, Kingston, Ontario, Canada.

PUBLICATIONS

Peer-Reviewed Journals

1. **Freeman BA**, R Sissenstein, TT McManus, JE Woodward, IM Lee and JB Mudd. Lipid composition and lipid metabolism of *Spiroplasma citri*. *J Bacteriol* 125:946-954, 1976.
2. **Freeman BA**, K Platt-Aloia, JB Mudd and WW Thomson. Ultrastructural and lipid changes associated with the aging of citrus leaves. *Protoplasma* 94:221-234, 1978.
3. **Freeman BA**, MC Sharman and JB Mudd. Reaction of ozone with phospholipid vesicles and human erythrocyte ghosts. *Arch Biochem Biophys* 197:264-272, 1979.
4. **Freeman BA** and WS Lynn. Fatty acid metabolism and secretion by activated rabbit alveolar macrophages. *Biochim Biophys Acta* 620:528-537, 1980.
5. Lynn WS, C Mukherjee and **BA Freeman**. Linoleic acid: A specific cytotoxin for macrophages. *Prog Lipid Res* 20:663-670, 1981.
6. **Freeman BA** and JB Mudd. Reaction of ozone with human erythrocyte sulfhydryls. *Arch Biochem Biophys* 208:212-220, 1981.
7. **Freeman BA** and JD Crapo. Hyperoxia increases oxygen radical production in rat lungs and lung mitochondria. *J Biol Chem* 256:10986-10992, 1981.
8. Hayatdavoudi G, JJ O'Neil, BE Barry, **BA Freeman** and JD Crapo. Pulmonary injury in rats following continuous exposure to 60% O₂ for 7 days. *J Applied Physiol: Resp Env Ex Physiol* 51:1220-1231, 1981.
9. **Freeman BA**, MK Topolosky and JD Crapo. Hyperoxia increases oxygen radical production in rat lung homogenates. *Arch Biochem Biophys* 216:477-484, 1982.
10. Turrens JF, **BA Freeman**, JG Levitt and JD Crapo. The effect of hyperoxia on superoxide production by lung submitochondrial particles. *Arch Biochem Biophys* 217:401-410, 1982.
11. Turrens JF, **BA Freeman** and JD Crapo. Hyperoxia increases H₂O₂ release by lung mitochondria and microsomes. *Arch Biochem Biophys* 217:411-421, 1982.
12. **Freeman BA** and JD Crapo. Biology of disease: Free radicals and tissue injury. *Lab Invest* 47:412-426, 1982.
13. Crapo JD, **BA Freeman**, BE Barry, JF Turrens and SL Young. Mechanisms of hyperoxic injury to the pulmonary microcirculation. *The Physiologist* 26:170-176, 1983.
14. **Freeman BA**, SL Young and JD Crapo. Liposome-mediated augmentation of superoxide dismutase in endothelial cells prevents oxygen injury. *J Biol Chem* 258:12534-12542, 1983.
15. Crapo JD, T Yusa and **BA Freeman**. Production of toxic oxygen species by high oxygen pressures and modulation of their effects on lung and brain by liposome encapsulated antioxidant enzymes. *Jap J Occup Environ Health* 6:28-29, 1984.

16. Turrens JF, JD Crapo and **BA Freeman**. Protection against oxygen toxicity by intravenous injection of liposome-entrapped catalase and superoxide dismutase. *J Clin Invest* 73:87-95, 1984.
17. Tanswell AK and **BA Freeman**. Pulmonary antioxidant enzyme maturation in the fetal and neo-natal rat. I. Developmental profiles. *Pediat Res* 18:584-587, 1984.
18. Tanswell AK and **BA Freeman**. Differentiation-arrested rat fetal lung in primary monolayer culture: Antioxidant enzyme activity. *Exp Lung Res* 6:149-158, 1984.
19. Tanswell AK and **BA Freeman**. Pulmonary antioxidant enzyme maturation in the fetal and neo-natal rat. II. The influence of maternal iron supplements upon fetal lung catalase activity. *Pediat Res* 18:871-874, 1984.
20. Yusa T, JD Crapo and **BA Freeman**. Hyperoxia enhances lung and liver nuclear superoxide generation. *Biochim Biophys Acta* 798:167-174, 1984.
21. Yusa T, JD Crapo and **BA Freeman**. Liposome-mediated augmentation of brain SOD and catalase inhibits CNS O₂ toxicity. *J Appl Physiol* 57:1674-1681, 1984.
22. Drysdale DB, **BA Freeman**, JD Crapo, PC Burger, DB Chandler and GK Klintworth. Liposomes and retrorenal fibroplasia. *Proceedings of the University of Otago Medical School* 62:21-23, 1984.
23. Rosen GR and **BA Freeman**. Detection of superoxide in endothelial cells. *Proc Natl Acad Sci* 81:7269-7273, 1984.
24. Burger PC, DB Chandler, DB Drysdale, Y Tano, **BA Freeman** and GK Klintworth. Scanning electron microscopy of vascular casts in experimental ocular vasoproliferation. *Scanning Electron Microscopy* 4:1893-1898, 1984.
25. McDonald RJ, EM Berger, CW White, **BA Freeman** and JE Repine. Effect of superoxide dismutase encapsulated in liposomes or conjugated with polyethyleneglycol on neutrophil bactericidal activity in vitro and bacterial clearance in vivo. *Am Rev Resp Dis* 131:633-637, 1985.
26. **Freeman BA**, JF Turrens, Z Mirza, JD Crapo and SL Young. Modulation of oxidant lung injury by using liposome-entrapped superoxide dismutase and catalase. *FASEB J* 44:2591-2595, 1985.
27. Bishop CT, JD Crapo and **BA Freeman**. Free radical injury to cultured aortic endothelial cells and lung fibroblasts: Modulation by culture medium and free radical scavengers. *In Vitro* 21:229-236, 1985.
28. **Freeman BA**, RJ Mason, MC Williams and JD Crapo. Antioxidant enzyme activity in type II cells after exposure of rats to hyperoxia. *Exp Lung Res* 10:203-222, 1986.
29. **Freeman BA**, GR Rosen and MJ Barber. Superoxide perturbation of the organization of vascular endothelial cell membranes. *J Biol Chem* 261:6590-6593, 1986.
30. Yusa T, **BA Freeman** and JD Crapo. Increased intracellular oxygen free radical generation by hyperoxia and the role of antioxidant enzymatic defenses. *Jap J Anesthesiol* 33:1299-1310, 1986.
31. Slot JW, HJ Geuze, **BA Freeman** and JD Crapo. Intracellular localization of the copper, zinc and manganese superoxide dismutases in rat and liver parenchymal cells. *Lab Invest* 55:363-371, 1986.
32. Tanswell AK and **BA Freeman**. Liposome-entrapped antioxidant enzymes prevent lethal oxygen toxicity in the newborn rat. *J Appl Physiol* 63:347-352, 1987.
33. Yusa T, JS Beckman, JD Crapo and **BA Freeman**. Hyperoxia increases hydrogen peroxide production by brain in vivo. *J Appl Physiol* 63:353-358, 1987.

34. Buckley BJ, AK Tanswell and **BA Freeman**. Liposome mediated augmentation of catalase in type II alveolar epithelial cells protects against hydrogen peroxide injury. *J Appl Physiol* 63:359-367, 1987.
35. Beckman JS, RL Minor and **BA Freeman**. Augmentation of antioxidant enzymes in vascular endothelium. *Free Radical Biol Med* 2:359-365, 1987.
36. Beckman JS, RL Minor, CW White, GM Rosen, JR Repine and **BA Freeman**. Superoxide dismutase and catalase conjugated to polyethylene glycol increases endothelial enzyme activity and oxidant resistance. *J Biol Chem* 263:6884-6892, 1988.
37. Ackerman AD, JC Fackler, CM Tuck-Muller, MM Tarpey, **BA Freeman** and MC Rogers. Partial monosomy 21, diminished activity of superoxide dismutase, and pulmonary oxygen toxicity. *N Engl J Med* 318: 666-1669, 1988.
38. Lell WA, JW Kirklin and **BA Freeman**. Case conference. A 44-year-old attorney was transferred from another hospital in cardiogenic shock for transplant evaluation. *Cardiothorac Anesth*. 2(4):555-66, 1988.
39. Tamura Y, L Chi, EM Driscoll, Jr., PT Hoff, **BA Freeman**, KP Gallagher and BR Lucchesi. Superoxide dismutase conjugated to polyethylene glycol provides sustained protection against myocardial ischemia/reperfusion injury in the canine heart. *Circ Res* 63:944-959, 1988.
40. Panus PC, J Shearer and **BA Freeman**. Pulmonary metabolism of reactive oxygen species. *Exp Lung Res* 14:959-976, 1988.
41. Liu TH, JS Beckman, **BA Freeman**, EL Hogan and CY Hsu. Polyethylene glycol-conjugated superoxide dismutase and catalase reduce ischemic brain injury. *Am J Physiol: Heart Circ. Physiol.* 256: H589-593, 1989.
42. White CW, JH Jackson, A Abuchowski, GM Kazo, RF Mimmack, **BA Freeman**, JM McCord and JE Repine. Treatment with polyethylene glycol-attached superoxide dismutase and catalase prevents pulmonary oxygen toxicity in rats. *J Appl Physiol* 66:584-590, 1989.
43. Tanswell AK, L Wong, F Possmayer and **BA Freeman**. The preterm rat: A model for studies of acute and chronic neonatal lung disease. *Pediat Res* 25:525-590, 1989.
44. Matalon SM, JS Beckman, ME Duffey and **BA Freeman**. Oxidant inhibition of epithelial active sodium transport. *Free Radic Biol Med* 6:557-564, 1989.
45. Beckman JS, DA Parks, J Pearson, P Marshall and **BA Freeman**. A sensitive fluorometric assay for measuring xanthine dehydrogenase and oxidase in tissues. *Free Radic Biol Med* 6:607-615, 1989.
46. Panus PJ, SM Matalon and **BA Freeman**. Responses to type II pneumocyte antioxidant enzymes to normoxic and hyperoxic culture. *In Vitro* 25:821-829, 1989.
47. Long MM, V King, KU Prasad, **BA Freeman** and DW Urry. Elastin repeat peptides as chemoattractants for bovine aortic endothelial cells. *J Cell Physiol* 140:512-518, 1989.
48. Royall JA, RL Berkow, JS Beckman, MK Cunningham, S Matalon and **BA Freeman**. Tumor necrosis factor and interleukin 1 alpha increase vascular endothelial cell permeability. *Am J Physiol: Lung Cell Mol Biol* 257:L399-L410, 1989.
49. Beckman JS, TW Beckman, J Chen, PA Marshall and **BA Freeman**. Apparent hydroxyl radical production by peroxy nitrite: Implications for endothelial injury from nitric oxide and superoxide. *Proc Natl Acad Sci* 87:1620-1624, 1990.

50. Yokoyama Y, JS Beckman, TK Beckman, JK Wheat, TG Cash, **BA Freeman** and DA Parks. Circulating xanthine oxidase: potential mediator of ischemic injury. *Am J Physiol: Gastrointest Liver Physiol* 258:G564-G570, 1990.
51. Tanswell AK, DM Olson and **BA Freeman**. Liposome-mediated augmentation of antioxidant defenses in fetal rat pneumocytes. *Am J Physiol: Lung Cell Mol Biol* 258:L165-L172, 1990.
52. Tanswell AK, DM Olson and **BA Freeman**. Response of fetal rat lung fibroblasts to elevated oxygen concentrations after liposome-mediated augmentation of antioxidant enzymes. *Biochim Biophys Acta* 1044:269-274, 1990.
53. Matalon S, BA Holm, RR Baker, MK Whitfield and **BA Freeman**. Characterization of antioxidant activities of pulmonary surfactant mixtures. *Biochim Biophys Acta* 1035:121-127, 1990.
54. Baker RR, PC Panus, BA Holm, PC Engstrom, **BA Freeman** and S Matalon. Endogenous xanthine oxidase-derived O₂ metabolites inhibit surfactant metabolism. *Am J Physiol: Lung Cell Mol Biol* 258:L328-L334, 1990.
55. Radi R, KM Bush, TP Cosgrove and **BA Freeman**. Reaction of xanthine oxidase-derived oxidants with lipid and protein of human plasma. *Arch Biochem Biophys* 286:117-125, 1991.
56. Panus PC, B Burgess and **BA Freeman**. Characterization of type II alveolar epithelial cell xanthine oxidase. *Biochim Biophys Acta* 1091:303-309, 1991.
57. Radi R, JS Beckman and **BA Freeman**. Peroxynitrite oxidation of sulphydryls: The cytotoxic potential of endothelial-derived superoxide and nitric oxide. *J Biol Chem* 266:4244-4250, 1991.
58. Radi R, JF Turrens and **BA Freeman**. Cytochrome c-catalyzed membrane lipid peroxidation by hydrogen peroxide. *Arch Biochem Biophys* 288:118-125, 1991.
59. Radi R, JS Beckman, KM Bush and **BA Freeman**. Peroxynitrite-induced membrane lipid peroxidation: the cytotoxic potential of superoxide and nitric oxide. *Arch Biochem Biophys* 288:481-487, 1991.
60. Radi R, JF Turrens, LY Chang, KM Bush, JD Crapo and **BA Freeman**. Detection of catalase in rat heart mitochondria. *J Biol Chem* 266:22028-22034, 1991.
61. Han RNN, S Buch, **BA Freeman**, M Post, and AK Tanswell. Platelet-derived growth factor and growth-related genes in rat lung II. Effect of exposure to 85% O₂. *Am J Physiol: Lung Cell Mol Biol* 262:140-146, 1992.
62. Beckman JS, SL Lindsay, TH Liu, TH Xu, P Marshall, JK Thompson, DA Parks, **BA Freeman** and CY Hsu. Role of xanthine dehydrogenase and oxidase in focal cerebral ischemic injury to rat. *Am J Physiol: Heart Circ Physiol* 261:H2051-H2057, 1991.
63. Royall JA, PD Gwin, DA Parks and **BA Freeman**. Responses of vascular endothelial oxidant metabolism to lipopolysaccharide and tumor necrosis factor- α . *Arch Biochem Biophys* 294:686-694, 1992.
64. Panus PC, SW Wright, PH Chumley, R Radi and **BA Freeman**. The contribution of vascular endothelial xanthine dehydrogenase/oxidase to oxygen-mediated cell injury. *Arch Biochem Biophys* 294:695-702, 1992.
65. Stone KC, RR Mercer, **BA Freeman**, L-Y Chang and JD Crapo. Distribution of lung cell numbers and volumes between alveolar and nonalveolar tissue. *Am Rev Respir Dis* 146:454-456, 1992.

66. Hamvas A, R Palazzo, L Kaiser, J Cooper, T Shuman, M Velazquez, **BA Freeman** and D Schuster. Inflammation and oxygen free radical formation during pulmonary ischemia-reperfusion injury. *J Appl Physiol* 72:621-628, 1992.
67. Radi R, K Bush and **BA Freeman**. The role of cytochrome c and mitochondrial catalase in hydroperoxide-induced heart mitochondrial lipid peroxidation. *Arch Biochem Biophys* 300:409-415, 1993.
68. Radi R, TP Cosgrove, JS Beckman and **BA Freeman**. Peroxynitrite-induced luminol chemiluminescence. *Biochem J* 290:51-57, 1993.
69. S Tan, E Dickens, Y Yokoyama, E Dickens, TG Cash, **BA Freeman**, and D Parks. Xanthine oxidase activity in the circulation of rats following hemorrhagic shock. *Free Radic Biol Med* 15: 407-414, 1993.
70. Panus PC, R Radi, PH Chumley and **BA Freeman**. Detection of cellular hydrogen peroxide release. *Free Radic Biol Med*, 14:217-233, 1993.
71. Baker RR, L Czopf, T Jilling, **BA Freeman**, KL Kirk and S Matalon. Quantitation of alveolar distribution of liposome-entrapped antioxidant enzymes. *Am J Physiol: Lung Cell Mol Biol* 263:L585-L594, 1992.
72. White CR, TA Brock, L-Y Chang, J Crapo, P Briscoe, D Ku, WA Bradley, SH Gianturco, J Gore, **BA Freeman**, MM Tarpey. Superoxide and peroxynitrite in atherosclerosis. *Proc Natl Acad Sci* 91:1044-1048, 1994.
73. Paler-Martinez A, PC Panus, PH Chumley, U Ryan, MM Hardy and **BA Freeman**. Endogenous xanthine oxidase does not significantly contribute to vascular endothelial production of reactive oxygen species. *Arch Biochem Biophys* 311:79-85, 1994.
74. Christie NA, AS Slutsky, **BA Freeman** and AK Tanswell. A critical role for thiol, but not ATP, depletion in 95% oxygen-mediated injury of preterm pneumocytes in vitro. *Arch Biochem Biophys* 313:131-138, 1994.
75. Rubbo H, R Radi, M Trujillo, R Telleri, B Kalyanaraman, S Barnes, M Kirk and **BA Freeman**. Nitric oxide regulation of superoxide and peroxynitrite-dependent lipid peroxidation: Formation of novel nitrogen-containing oxidized lipid derivatives. *J Biol Chem* 265:26066-26075, 1994.
76. Munzel T, H Sayegh, **BA Freeman**, MM Tarpey and DG Harrison. Evidence for enhanced vascular superoxide anion production in nitrate tolerance: A novel mechanism underlying tolerance and cross-tolerance. *J Clin Invest* 95:187-194, 1995.
77. Moore AM, S Buch, RNN Han, **BA Freeman**, M Post and AK Tanswell. Altered expression of collagen I, transforming growth factors- β 1 and related genes in rat lung exposed to 85% oxygen. *Am J Physiol: Lung Cell Mol Physiol* 268:L78-84, 1995.
78. Gutierrez HH, BR Pitt, M Brookens, SC Watkins, C Lowenstein, I Caniggia, P Chumley, A Rivera and **BA Freeman**. Pulmonary alveolar epithelial inducible nitric oxide synthase gene expression: regulation by inflammatory mediators. *Am J Physiol: Lung Cell Mol Physiol* 268:L501-L508, 1995.
79. Briscoe P, I Caniggia, A Graves, B Benson, L Huang, AK Tanswell and **BA Freeman**. Delivery of superoxide dismutase to pulmonary epithelium via pH-sensitive liposomes. *Am J Physiol: Lung Cell Mol Physiol* 268:L374-L380, 1995.

80. Buch S, RNN Han, J Liu, A Moore, **BA Freeman**, M Post and AK Tanswell. Basic fibroblast growth factor and growth factor receptor gene expression 85% oxygen-exposed rat lung. *Am J Physiol: Lung Cell Mol Physiol* 268:L455-L464, 1995.
81. Rubbo H, S Parthasarathy, S Barnes, M Kirk, B Kalyanaraman and **BA Freeman**. Nitric oxide inhibition of lipoxygenase-dependent liposome and low-density lipoprotein oxidation: formation of novel nitrogen-containing oxidized lipid derivatives. *Arch Biochem Biophys* 324:15-25, 1995.
82. Nieves-Cruz B, A Rivera, J Cifuentes, G Pataki, S Matalon, WA Carlo, AK Tanswell and **BA Freeman**. Clinical surfactant preparations mediate SOD and catalase uptake by type II cells and lung tissue. *Am J Physiol: Lung Cell Mol Physiol* 270:L659-L667, 1996.
83. Alvarez B, H Rubbo, M Kirk, S Barnes, **BA Freeman** and Rafael Radi. Peroxynitrite-dependent tryptophan nitration. *Chem Res Toxicol* 9:390-396, 1996.
84. Rajagopalan S, S Kurz, T Münzel, M Tarpey, **BA Freeman**, KK Griendling, DG Harrison. Angiotensin II mediated hypertension in the rat increases vascular superoxide production via membrane NADH/NADPH oxidase activation: Contribution to alterations of vasomotor tone. *J Clin Invest* 97:1916-1923, 1996.
85. Gutierrez HH, P Chumley, A Rivera and **BA Freeman**. Nitric oxide regulation of superoxide-dependent lung cell injury: oxidant-protective actions of endogenously produced and exogenously administered nitric oxide. *Free Radic Biol Med* 21:43-52, 1996.
86. Poss WB, TP Huecksteadt, PC Panus, **BA Freeman** and JR Hoidal. Regulation of xanthine dehydrogenase and xanthine oxidase activity by hypoxia. *Am J Physiol: Lung Cell Mol Physiol* 270:L941-946, 1996.
87. Han RNN, VKM Han, S Buch, **BA Freeman**, M Post and AK Tanswell. Insulin-like growth factor-I and type I insulin-like growth factor receptor in 85% O₂-exposed rat lung. *Am J Physiol: Lung Cell Mol Physiol* 271: L139-149, 1996.
88. White CR, V Darley-Usmar, M McAdams, WR Berrington, J Gore, JA Thompson, DA Parks, MM Tarpey and **BA Freeman**. Circulating plasma xanthine oxidase contributes to vascular dysfunction in hyper-cholesterolemic rabbits. *Proc Natl Acad Sci* 93: 8745-8749, 1996.
89. Denicola A, **BA Freeman**, M Trujillo, and R Radi. Peroxynitrite reaction with carbon dioxide/bicarbonate: kinetics and influence on peroxynitrite-mediated oxidations. *Arch Biochem Biophys* 333:49-58, 1996.
90. Münzel T, S Kurz, S Rajagopalan, M Thoenes, WA Berrington, JA Thompson, **BA Freeman** and DG Harrison. Hydralazine prevents nitroglycerin tolerance by inhibiting activation of a membrane-bound NADH oxidase: a new action for an old drug. *J Clin Invest* 98:1465-1470, 1996.
91. Laursen JB, S Rajagopalan, Z Galis, M Tarpey, **BA Freeman** and DG Harrison. Role of superoxide in angiotension II-induced but not catecholamine-induced hypertension. *Circulation* 95:588-593, 1997.
92. Radi R, H Rubbo, K Bush and **BA Freeman**. Xanthine oxidase binding to glycosaminoglycans: Kinetics and superoxide dismutase interactions of the immobilized xanthine oxidase-heparin complexes. *Arch Biochem Biophys* 339:125-135, 1997.
93. Tan S, M McAdams, J Royall, **BA Freeman** and DA Parks. Endothelial injury from a circulating mediator following rat liver ischemia. *Free Radic Biol Med* 24:427-434, 1997.

94. Capers Q IV, JB Laursen, T Fukui, S Rajagopalan, I Mori, P Lou, **BA Freeman**, WR Berrington, KK Griendling, DG Harrison, MS Runge, RW Alexander and WR Taylor. Vascular thrombin receptor regulation in hypertensive rats. *Circ Res* 80:838-844, 1997.
95. O'Donnell, VB, PH Chumley, N Hogg, A Bloodsworth, VM Darley-Usmar and **BA Freeman**. Nitric oxide inhibition of lipid peroxidation: Kinetics of reaction with lipid peroxy radicals and comparison with α -tocopherol. *Biochemistry* 36:15216-15223, 1997.
96. Eiserich JP, M Hristova, CE Cross, AD Jones, **BA Freeman**, B Halliwell and A van der Vliet. Formation of nitric oxide-derived inflammatory oxidants by myeloperoxidase in neutrophils. *Nature* 391:393-397, 1998.
97. Trujillo M, MN Alvarez, G Peluffo, **BA Freeman** and R Radi. Xanthine oxidase-mediated decomposition of S-nitrosothiols. *J Biol Chem* 273:7828-7834, 1998.
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99. Nielsen VG, MS Baird, ML McAdams and **BA Freeman**. Desflurane increases pulmonary alveolar-capillary membrane permeability after aortic occlusion-reperfusion in rabbits. *Anesthesiology* 88:1524-34, 1998.
100. Houston M, P Chumley, R Radi, H Rubbo and **BA Freeman**. Xanthine oxidase reaction with nitric oxide and peroxynitrite. *Arch Biochem Biophys* 355:1-8, 1998.
101. O'Donnell VB, JP Eiserich, PH Chumley, MJ Jablonsky, NR Krishna, M Kirk, S Barnes, VM Darley-Usmar and **BA Freeman**. Nitration of unsaturated fatty acids by nitric oxide-derived reactive nitrogen species: peroxynitrite, nitrous acid, nitrogen dioxide, and nitronium ion. *Chem Res Toxicol* 12:83-92, 1999.
102. Houston M, A Estevez, P Chumley, M Aslan, S Marklund, DA Parks and **BA Freeman**. Binding of xanthine oxidase to vascular endothelium. *J Biol. Chem* 274:4985-4994, 1999.
103. Alvarez B, G Ferrer-Sueta, **BA Freeman**, and R Radi. Kinetics of peroxynitrite reaction with amino acids and human serum albumin. *J Biol Chem* 274:842-848, 1999.
104. Eiserich JP, AG Estévez, TD Bamberg, YZ Ye, PH Chumley, JS Beckman and **BA Freeman**. Microtubule dysfunction by post-translational nitrotyrosination of α -tubulin: A nitric oxide-dependent mechanism of cellular injury. *Proc Natl Acad Sci USA* 96:6365-6370, 1999.
105. Tarpey MM, White CR, E Suarez, G Richardson, R Radi and **BA Freeman**. Chemiluminescent detection of oxidants in vascular tissue. Lucigenen but not coelenterazine enhances superoxide formation. *Circ Res* 84:1203-1211, 1999.
106. O'Donnell VB, KB Taylor, S Parthasarathy, H Kuhn, D Koesling, A. Fribe, A Bloodsworth, VM Darley-Usmar and **BA Freeman**. 15-Lipoxygenase catalytically consumes nitric oxide and impairs activation of guanylate cyclase. *J Biol Chem* 274:20083-20091, 1999.
107. Luo X, NA Christie, MA McLaughlin, R Belcastro, L Sedlackova, J Cabacungan, **BA Freeman** and AK Tanswell. H_2O_2 mediates O_2^- toxicity in cultured fetal rat distal lung epithelial cells. *Free Radic Biol Med* 26:1357-1368, 1999.
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111. Ballinger SW, C Patterson, C-N Yan, R Doan, DL Burow, FM Yakes, B Van Houten, CA Ballinger, **BA Freeman** and MS Runge. Superoxide, hydrogen peroxide, nitric oxide and peroxynitrite-induced mitochondrial DNA damage and dysfunction in vascular endothelial and smooth muscle cells. *Circ Res* 86:960-966, 2000.
112. Corbacho AM, G Nava, JP Eiserich, G Noris, Y Macotela, I Struman, GM de la Escalera, **BA Freeman** and C Clapp. Proteolytic cleavage confers prolactin with NO synthase-inducing activity. *J Biol Chem* 275:13183-13186, 2000.
113. Bloodsworth A, V O'Donnell and **BA Freeman**. Nitric oxide regulation of free radical- and enzyme-mediated lipid and lipoprotein oxidation. *Arterioscler Thromb Vasc Biol* 20:1707-1715, 2000.
114. Cassina AM, R Hodara, JM Souza, L Thomson, L Castro, H Ischiropoulos, **BA Freeman** and R Radi. Cytochrome c nitration by peroxynitrite. *J Biol Chem* 275:21409-21415, 2000.
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PROFESSIONAL ACTIVITIES

TEACHING:

Updated: 02/09

Bruce A. Freeman, PhD
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Past Trainees

Predoctoral Trainees	Dates	Research Project	Current Position
Cynthia Karfias, B.S.	1985	Chemical modification of SOD for enhanced intracellular delivery	Assoc. Prof., Medicine Duke Univ Med Cntr, Durham
Robert Minor, B.S.	1986	Polyethyleneglycol-mediated chemical modification of SOD and its pharmacology	Assoc. Prof., Medicine Univ. Iowa,
John Shearer, M.D.	1990	Lung type II cell oxygen radical metabolism	Physician, Health South Hospital, Birmingham
Graduate Trainees	Dates	Research Project	Current Position
Andres Paler-Martinez, PhD	1988-95	Sources of vascular endothelial oxygen radical production	Research Associate Professor, Univ CA, Berkeley
Page Briscoe-McKenzie, PhD	1988-94	Development of pH-sensitive liposomes for pulmonary drug delivery	Oak Ridge Inst. For Science & Medicine, Oak Ridge TN.
Michelle McAdams-Houston, PhD	1991-97	Endothelial oxygen radical metabolism Circulating XO: cell binding characteristics	Research Fellow, Emory Univ. Atlanta, GA
Rafael Radi, MD, PhD	1990-93	Free radical chemistry of nitric oxide and xanthine oxidase-glycosaminoglycan interactions	Professor, Dept Biochemistry Univ of the Republic, Montevideo, Uruguay
Homero Rubbo, PhD	1991-93	Nitric oxide mediated fatty acid nitration	Professor, Dept Biochemistry Univ of the Republic, Montevideo, Uruguay
Wm. Berrington, MD, PhD	1993-98	Oxidant production by inducible nitric oxide synthase activation of xenobiotics	Pulmonary Fellow University of Washington
Allison Bloodsworth, PhD	1997-2001	Nitric oxide regulation of plasma lipoprotein oxidation	Research Assoc., Dept. Medicine Washington Univ, St Louis, MO
Mutay Aslan, MD, PhD	1997-2002	Nitric oxide-oxygen radical reactions in sickle cell disease.	Asst. Prof, Akdeniz Univ Antalya, Turkey
Postdoctoral Trainees	Dates	Research Project	Current Position
Maury Topolosky, MD	1981-82	Oxygen radical production by hyperoxic lung	Physician, Christie Clinic, Champaign, IL
Toshika Yusa, MD	1982-84	Cerebrovascular hydrogen peroxide production and CNS drug delivery	Chair, Dept Anesthesiology Univ of Ryukyu, Okinawa, Japan
Julio Turrens, PhD	1982-84	Mitochondrial oxidant production and development of liposomal antioxidant delivery systems	Professor, Dept Biochemistry Univ of So Alabama, Mobile
Clark Bishop, MD	1983-84	Oxygen radical production by cultured lung cells	Physician, Utah Valley Medical Center, Provo, UT

Douglas Drysdale, PhD	1983	Detection of microsomally-derived oxygen radicals	Professor, Dept of Physiology Univ of New Zealand, Otago
Carl White, MD	1984-85	Hyperoxia-induced pulmonary free radical production and antioxidant responses	Professor, Dept Pediatrics, Natl Jewish Center, Denver
Joseph Beckman, PhD	1985-88	Cerebrovascular free radical production vascular nitric oxide and oxidant reactions	Professor, Dept Biochemistry Oregon State Univ
Gerald Campbell, MD	1985	Histopathology of oxygen radicals in brain	Professor, Dept Pathology UT Med Branch, Galveston
Barbara Buckley, PhD	1986-87	Oxygen radical production by and injury to the alveolar epithelium	Assoc Professor, Dept Pharmacol, Duke University
A. Keith Tanswell, MD	1986-87	Oxygen radical injury to fetal lung	Professor, Dept Pediatrics Hosp for Sick Children, Toronto
Sadis Matalon, PhD	1987	Oxygen radical-induced defects in cell ion transport	Prof., Depts Anesthesiology, Physiol & Pediatrics, UAB
Susan Lindsay, MD	1988-89	Ischemia-induced oxygen radical injury to the brain	Staff Anesthesiologist, St. Bartholemew Hosp, London
James Royall, MD	1988-90	Regulation of vascular oxidant metabolism by inflammatory cytokines	Professor, Dept Pediatrics Univ Oklahoma, Oklahoma City
Peter C Panus, PhD	1987-92	Oxygen radical production by cellular and vascular xanthine oxidase	Prof, Dept of Allied Health, E.Tenn. State Univ, Johnson City,
Bedford Nieves, MD	1992-94	Pulmonary surfactant-mediated antioxidant delivery to lung cells	Physician, Dept Pediatrics, Children's Hosp, Houma, LA
Hector Gutierrez, MD	1992-95	Anti-inflammatory actions of nitric oxide	Assoc Professor, Dept Pediatrics, UAB
C. Roger White, PhD	1994-96	Oxygen radical-nitric oxide reactions in hypertensive vascular disease.	Professor, Dept Medicine, UAB
Homero Rubbo, PhD	1993-96	Nitric oxide regulation of lipid and lipoprotein oxidation	Prof Dept Biochemistry, Univ Republic, Montevideo, Uruguay
Val O'Donnell, PhD	1996-98	Oxidized lipid-nitric oxide adduct formation, NO regulation of LOX/COX	Assoc. Prof, Dept. of Biochem Univ. of Wales, Cardiology Res. Inst. Cardiff, U.K.
Jeffery Schultz, PhD	1997-98	Myeloperoxidase-mediated-tyrosine nitration	Assoc Prof., Dept Chemistry, Pacific Lutheran Univ, Tacoma, Washington
Jason Eiserich, PhD	1998- 2001	Peroxidase-nitric oxide reactions and host defense mechanisms	Assistant Professor, University of California at Davis
Laura Castro, MD, PhD	1999- 2002	Mitochondrial oxidant-nitric oxide reactions and apoptotic signaling	Assoc Professor, Univ de la Republica, Montevideo, Uruguay

Stephan Baldus, MD	1999-2002	Peroxidase-dependent tissue injury in vascular diseases	Asst Prof, Dept Cardiology Univ of Hamburg, Germany
Don Gun Lim, MD, PhD	2001-2003	Vascular signaling properties of nitric oxide nitrated fatty acid derivatives	Assoc Prof, Dept. Anesthesiology, Kyungpook Univ, Daegu, S. Korea
Jeff Schwartz, MD	2003-2005	Reactive species in the vascular dysfunction of sickle cell disease	Private practice pediatrics
Karen Isles, PhD	2003-2005	Protein kinase transduction of pulmonary and vascular nitrated fatty acid signaling	Research Assistant Professor UAB Dept Env Hlth Sci
John D. Lang, MD	2000-2005	CO ₂ modulation of oxidative inflammatory reactions in the lung	Assoc Professor, Anesthesiology, U. Washington
Laura Baker, PhD	2003-2007	Reaction kinetics between nitrated fatty acids and biomolecules	Postdoctoral Fellow – on family leave
Carlos Batthyany, MD, PhD	2004-2007	Protein regulation by electrophilic lipids	Assoc. Professor, Faculty of Sciences, Universidad de la Republica, Montevideo, Uruguay
Current trainees	Dates	Research projects	Current positions
Paul Baker, PhD	2002-	Tissue generation and cell signaling activities of nitrated fatty acids and complex lipids	Research Assistant Professor
Francisco Schopfer, PhD	2002-	Protein adduction by nitrated fatty acids	Research Assistant Professor
Marsha Cole, PhD	2005-	<i>In vivo</i> regulation of nitrated fatty acids	Postdoctoral Fellow
Gustavo Bonacci, PhD	2006-	Modulation of protein trafficking by nitrated fatty acids	Postdoctoral Fellow
Nicholas Khoo, PhD	2006-	Regulation of eNOS by nitrated fatty acids	Postdoctoral Fellow
Steven Woodcock, PhD	2007-	Organic synthesis of nitrated lipids	Postdoctoral Fellow
Tanya Rudolph, MD	2007-	Electrophilic signaling in atherosclerosis	Postdoctoral Fellow
Volker Rudolph, MD	2007-	Electrophilic signaling in ischemic heart disease	Postdoctoral Fellow
Chiara Cipollina, PhD	2008-	Anti-inflammatory actions of redox-derived electrophilic fatty acid derivatives	Postdoctoral Fellow
Alison Groeger	2004-	Nitro-fatty acids: Endogenous nitration and PPAR activation	Graduate Student

Course Lectures

Medical School Biochemistry - Intermediary metabolism, electron transport, mitochondria, inflammatory reactions

Dental School Biochemistry - Intermediary metabolism, electron transport, mitochondria inflammatory reactions

Cell and Molecular Biology - Oxidative metabolism, photosynthesis, membrane structure and function

Course Director - Graduate Series in biochemistry and cell biology of free radicals, oxidants and antioxidants.

Invited speaker / chairperson at conferences (last three years)

2005

Experimental Biology 2005

XXXV International Congress of Physiological Sciences

San Diego, CA

Mar. 31 – April 5, 2005

“Role of Reactive Oxygen and Nitrogen Species in Lung Injury and Diseases”

Wake Forest University

North Carolina

Guest Lecturer

April 12-14, 2005

Dinner Lecture for Sigma Xi Society - “Be Still My Beating Heart: Oxygen Regulation of Vascular Cell Communication”

Lecture for Dept. Biochemistry - Yellow Grease: Pluripotent Cell Signaling Activity of Vinyl Nitro Derivatives”

University of Miami

School of Medicine

Guest speaker for 6th Annual John E. Cunio, M.D. Memorial

Lecture, Medical Grand Rounds

April 20, 2005

“Redox Cell Signaling in Cardiovascular Disease: From the Bench to the Bedside”

April 21, 2005

Renal Grand Rounds

“Nitric Oxide – Friend and Foe in Vascular Inflammation”

2006

Joint 62nd Harden Conference/EMBO Workshop - NO; a radical in control.

Cirencester, UK

April 4-8, 2006

“Nitric oxide-dependent fatty acid nitration”

University of Pittsburgh Postdoctoral Association, Postdoctoral Data & Dine Symposium

Pittsburgh, PA

May 15, 2006

“Acquiring Extramural Research Support”

Department of Anesthesia and Surgery, Brigham and Women’s Hospital

Boston, MA

June 1, 2006

“O₂ regulation of cell signaling”

Biology Chemistry and Therapeutic Applications of Nitric Oxide

Fourth International Conference of the Nitric Oxide Society

Monterey, CA

June 25-29, 2006

"Nitric Oxide regulation of fatty acid signaling"

Endocrine Research Conference, University of Pittsburgh

Pittsburgh, PA

September 14, 2006

"Convergence of Nitric Oxide and Eicosanoid Signaling"

Oxidative Post-Translational Modifications of Proteins in Cardiovascular Disease

Boston, MA

October 4-6, 2006

"Nitric Oxide Regulation of Lipid Signaling."

Department of Cell Biology and Physiology, University of Pittsburgh

Pittsburgh, PA

October 31, 2006

"Adaptive Responses to Oxidative Inflammatory Stress"

Chair's Research Conference, Department of Surgery, University of Pittsburgh

Pittsburgh, PA

November 2, 2006

"NO-Derived Fatty Acid Nitration Products: Anti-Inflammatory Mediators"

NIH Symposium on Functional Genomics of Critical Illness and Injury

Bethesda, MD

November 13-14, 2006

"Nitroalkene regulation of protein function and gene expression – pluripotent cell signaling actions of NO-modified fatty acids"

American Society of Nephrology

Annual Meeting

San Diego, CA

November 16-19, 2006

Plenary lecture: "Redox reactions in cell signaling and inflammation"

Burke Medical Research Institute

White Plains, NY

December 5, 2006

"Fatty Acid Transduction of Nitric Oxide Signaling"

Office of Academic Career Development, University of Pittsburgh

Pittsburgh, PA

December 14, 2006

"Acquiring Extramural Research Support: A New Era with New Challenges"

2007

Department of Neurobiology, University of Pittsburgh

Pittsburgh, PA

January 9, 2007

"Convergence of fatty acid and nitric oxide cell signaling reactions"

Pulmonary, Allergy & Critical Care Medicine Joint Collaborative Conference, University of Pittsburgh School of Medicine

Pittsburgh, PA
February 20, 2007
“Convergence of NO and fatty acid signaling pathways”

University of Utah, Department of Medicine
Salt Lake City, UT
May 7, 2007
“Nitric Oxide Regulation of Lipid Signaling”

Frontiers in Biomedical Research
Nobel Foundation
Stockholm, Sweden
June 1, 2007
“Nitric Oxide, Nitrite and Redox Signaling”

American Society of Nephrology
Annual Meeting
San Francisco, CA
October 31 - November 2, 2007
“Transgenic Approaches to Lipid and Protein Nitration Reactions in Inflammatory Processes”

2008

University of South Alabama Department of Pharmacology
Mobile, AL
February 14, 2008
“Nitro-Fatty Acids - Transducers of Nitric Oxide and Redox Signaling”

University of Georgia Department of Biochemistry & Molecular Biology
Athens, GA
March 7, 2008
“Convergence of Nitric Oxide and Eicosanoid Signaling”

University of Massachusetts Medical School
Worcester, MA
April 16, 2008
“Convergence of Nitric Oxide and Lipid Signaling - Nitro Fatty Acid Derivatives”

Wake Forest Nitrogen Oxide Meeting
Farmington, PA
May 23, 2008
“Fishing for NO-derived Electrophiles and Catching Moby Dick”

NIEHS Council Meeting
Research Triangle Park, NC
May 29, 2008
“Xenobiotic and inflammatory-induced fatty acid nitration products – potent anti-inflammatory mediators”

Editorial Work

Associate Editor-American Journal of Physiology: Lung Cellular and Molecular Biology (1995-2001)
Associate Editor-Environmental and Nutritional Interactions (1997-present)
Editorial Board-Free Radical Biology and Medicine (1990-1998)
Editorial Board-Archives of Biochemistry and Biophysics (1993-1996)
Editorial Board-General Pharmacology: The Vascular System (1998-present)
Editorial Board-Nitric Oxide: Biology and Chemistry (1997- present)
Editorial Board-Critical Care Medicine (2000-present)
Editorial Board-Journal of Biological Chemistry (2007-present)

Advisory Board / Consulting

Oxis, Inc., Portland, OR
Aeolus, Inc., Research Triangle Park, NC
Glaxo/ Wellcome, Research Triangle Park, NC
Cardiome, Inc., Vancouver, BC
INO Therapeutics, Boston, MA

Service

1988-1990	American Lung Association Research Review Committee
1998-1990	Pathology A Study Section, NIH
1990-1994	Lung Biology and Pathology Study Section
1992-1996	American Heart Association - Alabama Affiliate Research Review Committee Guggenheim Foundation Medical Research Council of Canada Medical Research Council of England National Science Foundation NIH Reviewer Reserve Parker B. Francis Foundation United States-Israel Binational Science Foundation Veteran's Administration Wellcome Trust

RESEARCH

Key Research and Professional Accomplishments

- Definition of biochemical mechanisms of ozone toxicity to biological membranes and lung cells. It was observed that protein amino acid oxidation reactions predominated over ozonolysis of membrane lipid olefins as the principal pathogenic mechanism of ozone reaction.
- Devised novel techniques for measuring tissue and organelle production of reactive oxygen species and brought these strategies to bear to reveal the influence of intermediary metabolism, oxygen concentration and xenobiotic exposure on tissue oxidant production and injury.
- Developed new approaches for delivering antioxidants to critical sites of oxygen radical production and reaction, namely intracellular compartments and cell surfaces. Normally membrane impermeant macromolecules such as antioxidant enzymes were delivered using liposomal vectors, following polyethyleneglycol conjugation and following the bacterial expression of recombinant chimeric heparin-binding antioxidant enzymes that have a high affinity for cell surface proteoglycans.
- Pioneered the concept, with trainees JS Beckman and R Radi, that the inflammatory mediator and signal transduction molecule nitric oxide ($\cdot\text{NO}$) plays a profound role in accelerating oxidative/free radical injury via reaction with superoxide and the formation of peroxynitrite (ONOO^-).
- Defined the dual pro-oxidant and antioxidant roles that $\cdot\text{NO}$ displays with oxidizing lipids via oxidation reactions and inhibition of lipid radical chain propagation reactions. Current investigations in this area involve investigation of the roles that oxidized lipid- $\cdot\text{NO}$ reactions play in regulating cell $\cdot\text{NO}$ and eicosanoid signaling and mediation of cell signaling.
- Contributed to the concept that CO_2 chemically participates in the reactivity of O_2^- and $\cdot\text{NO}$ via reaction with ONOO^- and formation of the potent secondary oxidizing and nitrating species, nitrosoperoxocarbonate (ONOOCOO^-). Current investigations are directed toward defining the contribution of CO_2 to pulmonary oxidant injury, since permissive hypercapnia and the use of inhaled $\cdot\text{NO}$ as a pulmonary vasodilator is a widespread ventilatory strategy in critical care medicine.
- Entrepreneurial activities have included patenting of some of the previously noted novel antioxidant interventions. Other pursuits include serving as a cofounder of Oxis International, Portland, Oregon, a biotechnology company that is directed toward the pre-clinical and clinical development of low molecular weight antioxidants and antioxidant enzyme mimetics. Recently, Nitrolipids, Inc. has been founded to support the preclinical development of nitrated fatty acids as PPAR ligands and anti-inflammatory signaling mediators. Consulting, preclinical drug evaluation and clinical investigation is also provided for Aeolus, Inc. and Cardiome, Inc., companies interested in bringing antioxidant strategies to the clinical marketplace.
- Service to professional organizations includes past duty as the Treasurer and later, President of The Oxygen Society. Activities as President included recruiting a professional management team to oversee Society business/finances and organizing the negotiation of a contract between Elsevier and The Oxygen Society for the society journal, *Free Radical Biology and Medicine* and recruitment of new Associate Editors. This arrangement brought an additional \$1.2 million to the Society over the five year contract. During this term of office, the organization of two international meetings and workshops on free radical biology generated \$50,000 in revenue to The Oxygen Society and provided an additional \$45,000 for Young Investigator Research Awards to attendees. Established The Sunrise Free Radical School, now an integral part of the annual meeting of this society.
- Founded the Department of Anesthesiology Research Division at UAB in 1986 and the UAB Center for Free Radical Biology in 1996. The Anesthesiology Research Division consistently ranks in the top 10 nationally in anesthesiology department NIH funding.
- Mentored numerous clinical and basic science fellows that now thrive in prominent independent careers, in addition to the training of Ph.D. students. Five postdoctoral trainees now hold endowed professorships (Tanswell, Matalon, Beckman, Radi, Eiserich). Also, every research assistant that has worked in and then departed from my laboratory has advanced to graduate from professional schools, earning doctorates in medicine, dentistry and veterinary medicine (plus one patent attorney).
- Named in 2003 as one of the 100 “Most Highly Cited” authors in biology and biochemistry (ISI). Publication #49 is the sixth most highly cited publication in biology and biochemistry since citation analysis began in 1981. Publication #75 was editorialized as a “Hot Paper” by ISI/The Scientist soon after its publication and was the first report of the discovery of a novel class of endogenous anti-inflammatory compounds.

Extramural Research Support as Principal Investigator

<u>Funding Institution</u>	<u>Beginning</u>	<u>Ending</u>	<u>Total Direct Costs</u>
AMERICAN LUNG ASSOCIATION Oxygen Radical Production and Antioxidant Defenses of Lung Cells	7/1/82	6/31/84	\$30,000
NATIONAL HEART LUNG AND BLOOD INSTITUTE / NIH / R23 - HL29784 Vesicle Delivery of Antioxidant Enzymes to Lung Cells	1/1/83	12/31/85	\$112,500
NATIONAL INST OF NEUROLOGICAL COMMUN DIS STROKE / NIH-RO1-NS23700 Oxygen Radicals in Dysoxic Brain Injury	12/1/85	11/30/88	\$326,348
HEALTH EFFECTS INSTITUTE Oxidant Injury to the Alveolar Epithelium	11/1/85	9/30/88	\$310,572
DUPONT DE NEMOURS AND COMPANY Biochemical Actions of Azapropazone SMITH, KLINE & FRENCH Liposomal Delivery of Genetically Engineered Antiproteases	11/1/86 5/14/87	4/30/88 5/13/88	\$43,000 \$5,000
NATIONAL HEART, LUNG, AND BLOOD INSTITUTE / NIH / R01 - HL31192 Liposome Delivery of Antioxidant Enzymes to Lung Cells	4/1/84	3/31/89	\$456,057
STERLING-WINTHROP LAB. PEG-SOD Chemistry and Quality Control	9/2/88	12/31/90	\$100,000
STERLING-WINTHROP LAB Biochemical Markers of Tissue Free Radical Injury in Subjects Undergoing Aortocoronary Bypass Graft Surgery	12/1/90	12/31/91	\$139,430
STERLING DRUG INC. Biochemical Markers of Tissue Free Radical Injury in Subjects Undergoing Aortocoronary Bypass Graft Surgery	12/1/91	6/1/92	\$260,000
NATIONAL INST OF NEUROLOGICAL DISORDERS, STROKE /NIH/ R01-NS24275 Cerebrovascular Injury from Oxygen Radicals	7/1/87	6/30/92	\$747,294
NATIONAL HEART, LUNG, AND BLOOD INSTITUTE / NIH/R01 - HL48310 Reactive Species in Vascular Injury	12/1/88	11/30/93	\$1,026,078
NATIONAL HEART, LUNG, AND BLOOD INSTITUTE / NIH / R01 - HL48310 Reactive Species in Vascular Injury - Minority	7/1/92	3/31/95	\$220,375

<u>Funding Institution</u>	<u>Beginning</u>	<u>Ending</u>	<u>Total Direct Costs</u>
Supplement: Selwyn Vickers			
UNIVERSITY OF ALABAMA HEALTH SERVICES FOUNDATION New Shared Technology for the Study of Free Radical Biology-Stopped Flow Spectrometer	1/1/96	12/31/96	\$50,000
PARKER B. FRANCIS Foundation Reactive Species in Epithelial Injury	7/1/93	6/30/97	\$108,000
AMERICAN LUNG ASSOCIATION Mechanisms of Cigarette Smoke-Induced Protein Modification	7/1/96	6/30/97	\$20,000
COUNCIL FOR TOBACCO RESEARCH Nitric Oxide Regulation of Superoxide-Dependent Toxicity	1/1/95	12/31/97	\$246,250
UNIVERSITY OF ALABAMA HEALTH SERVICES FOUNDATION New Shared Technology for the Study of Free Radical Biology - Gas Chromatograph-Mass Spectrometer	9/1/97	8/31/98	\$40,000
FOGARTY INTERNATIONAL CENTER NIH / R03 - TW00489 Oxygen Radical-Nitrosothiol Interactions	9/1/95	8/31/98	\$74,820
NATIONAL HEART, LUNG, AND BLOOD INSTITUTE / NIH / P01- HL48676 Reactive Species in Vascular Injury: Project 3 Vascular Endothelial Oxidant Metabolism	9/30/92	12/31/99	\$1,228,743
NATIONAL HEART, LUNG, AND BLOOD INSTITUTE / NIH / P01 - HL48676 Reactive Species in Vascular Injury: Admin. Core	9/30/92	12/31/99	\$348,140
NATIONAL HEART, LUNG, AND BLOOD INSTITUTE / NIH / P01 - HL48676 Reactive Species in Vascular Injury: Tissue Culture Core	9/30/92	12/31/99	\$605,949
NATIONAL HEART, LUNG, AND BLOOD Reactive Species in Vascular Injury: Admin. Core INSTITUTE / NIH / R01 - HL51245 Lung Free Radical Metabolism and Injury	2/1/94	1/31/99	\$1,238,293
PARKER B. FRANCIS FOUNDATION Reactive Nitrogen Species In Pulmonary Disease	7/1/97	6/30/00	\$102,000
FOGARTY INTERNATIONAL CENTER NIH / R03 - TW00999 Oxygen Radicals and	9/1/98	8/31/01	\$74,820

<u>Funding Institution</u>	<u>Beginning</u>	<u>Ending</u>	<u>Total Direct Costs</u>
Nitric Oxide in Cell Signaling			
NATIONAL HEART, LUNG AND BLOOD INSTITUTE/NIH / RO1 - HL58115 Nitric Oxide Regulation of Vascular Oxidant Injury	9/1/97	8/30/02	\$1,238,293
NATIONAL HEART, LUNG, AND BLOOD INSTITUTE/ NIH / P60 - HL58418 UAB Comprehensive Sickle Cell Disease Ctr Project 3 - Reactive Species in Sickle Cell Disease	4/1/98	3/31/03	\$1,038,597
NATIONAL HEART, LUNG, AND BLOOD INSTITUTE/ NIH / RO1-HL64937 Nitric Oxide-Dependent Oxidative Lung Injury	12/01/99	11/30/04	\$1,250,000
NASA/Jet Propulsion Laboratory Mars Soil Reactivity-Biological Effects of Dust-Bound Superoxide	12/10/99	11/09/04	\$900,000
FOGARTY INTERNATIONAL CENTER NIH / R03 - TW05682 Nitric Oxide-Superoxide Interactions in Vascular Injury	06/01/01	08/31/05	\$96,000
PPTA Plasma Protein Therapeutics Association	01/01/02	12/31/03	\$70,000
NATIONAL HEART, LUNG AND BLOOD INSTITUTE/NIH / RO1 - HL58115 Nitric Oxide Regulation of Vascular Oxidant Injury	06/01/03	05/31/08	\$1,579,169
CARDIOME PHARMA CORP. Xanthine Oxidase Inhibition and Its Incidence on Coronary Vasomotion Performance	01/01/03	12/31/03	\$89,900
PHILIP MORRIS RESEARCH MANAGEMENT GROUP Albumin-An Intravascular Indicator of Reactive Inflammatory Mediators	05/01/03	04/30/06	\$272,250
NIH RO1HL64937-05 Nitric Oxide-Dependent Oxidative Lung Injury	04/01/05	03/31/10	\$1,356,000
R03 TW007431-01 – NIH Fogarty Anti Inflammatory Properties of Cholestryl Linoleate-Derived Nitrated Lipids	02/01/06	02/28/09	\$94,248

***Dr. Freeman has also served as a participating co-investigator with colleagues on other unlisted private sector, foundation and NIH/Federally-funded projects totaling ~\$10,000,000, and has served as a mentor for young investigator training grants totaling ~\$750,000.**